Please amend the application as follows:

IN THE SPECIFICATION:

Please amend the specification between the term "DESCRIPTION" and the term "FIELD OF THE INVENTION" in order to add the appropriate continuing data:

D1 -- This application is the §371 national phase application of PCT International Application no. PCT/IT99/00356, filed 8 November 1999, which claims, under §119(a), benefit of Italian Application RM98A000694, filed 6 November 1998. --

Please amend the specification at page 1, lines 10-13, as follows:

D2 An important aspect in the development of ~~the~~ gene therapy is the development of vectors capable of introducing genetic material into the target cells.

Please amend the specification at page 1 line 33 through page 2, line 4, as follows:

D3 This is due to some interesting characteristics of the Adenoviruses (Ad), which constitute a DNA virus family (the ones infecting ~~the~~ human beings have been classified in 57 serotypes), ~~characterised~~ characterized by an icosahedral capsid lacking an outer coat: they are highly infective but relatively innocuous, primarily infect ~~hepitelial~~ epithelial cells but can also infect cells of other tissues, regardless of their being in active replication phase.

Please amend the specification at page 2 lines 6-10, as follows:

D4 Moreover, it has been proved that human DNA inserts can be efficiently transferred into ~~hepitelial~~ epithelial human cells through Ad infection (Horvitz, "Adenoviridae and their replication" in Virology, Field and Knipe, ed. Raven Press, NY; 1990; pages 1679-1740).

Please amend the specification at page 3 lines 6-10, as follows:

D5 In the 40 years following the first isolation, following the ~~characterisation~~ characterization of Ad viruses, the relevant modifications that made them efficient carriers for the transfer of genic material have been progressively ~~get ready~~ developed.

Please amend the specification at page 3 lines 25-29, as follows:

D6 An increase of the size of the ~~etherologous~~ heterologous gene to be inserted and the restriction of the propagation of the recombinant viruses in cell lines that complement such defect because they constitutionally express genes of the viral E1 region, have ~~bee~~ been obtained.

Please amend the specification at page 4 lines 10-16, as follows:

Vectors differently combining E1, E2, E3, and/or E4 ~~deletion~~ deletions have been demonstrated to be less cytotoxic *in vitro* and more stable in mouse liver than the classic ΔE1 first generation vectors (Gao, G-P. 1996 J.Virol 70:8934-8943; Dedieu, J-F. 1997 J.Virol. 71:4626-4637; Gorziglia, M.I. 1996 J. Virol. 70:4173-4178; Amalfitano, A. 1998 J. Virol. 72:926-933).

Please amend the specification at page 6 lines 19-21, as follows:

In prior art there are several ~~description~~ descriptions of cells expressing one or more viral proteins (see for instance ~~Wo 98/13499~~ WO98/13499)

Please amend the specification at page 6 lines 23-29, as follows:

However, according to ~~these~~ this strategy, it is extremely difficult to satisfactorily produce the exact co-ordination of the events between the viral DNA replication and the expression of the structural proteins that in the natural infection lead to the massive production of viral ~~particle~~ particles typical of the lytic phase.

Please amend the specification at page 9 lines 4-9, as follows:

An example is given by the tetracycline promoter, which is the preferred one, even if ~~promoter~~ promoters regulated by the presence of other inductors like ecdysone, rapamycin, RU486, dexamethasone or heavy metal like Zn or Cd, are suitable as ~~wheel~~ well.

Please amend the specification at page 13 lines 9-12, as follows:

Further ~~case~~ cases are the ones wherein the viral region present in the first genic unit is operatively linked to at least one regulatory element enabling the tight control of ~~their~~ it's expression;

Please amend the specification at page 13 lines 26-30, as follows:

;the cells in which at ~~lest~~ least one of the non-structural regions in the second genic unit are totally or partially derived from adenovirus genome, preferably human adenovirus, preferably AD2 or AD5 serotype adenoviruses.

Please amend the specification at page 13 line 35 through page 14 line 2, as follows:

D13

Further ~~case~~ cases of interest are constituted by the cells in which the adenovirus genome of the first genic unit is derived totally or partially from adenovirus genome of mammalian adeniviruses, preferably human adenoviruses preferably AD2 and AD5 serotype adenovirus.

Please amend the specification at page14 lines 19-22, as follows:

D14

Further, ~~al~~ all the above described cells can be eukaryotic cells, preferably mammalian, preferably of humans, and in this latter case also preferably cells permissive for the Adenovirus replication.

Please amend the specification at page 16 lines 14-24, as follows:

D15

Pharmaceutically acceptable carriers are the ones well known in the art, i.e. sterile aqueous solutions which can contain the active principle only or can further include buffer such as sodium phosphate at physiological pH value, and/or physiological saline such as phosphate buffered ~~salin~~ saline. In addition, other excipients like a wetting or emulsifying agent, dissolution promoting agent, pH buffering agent, ~~stabilisers~~ stabilizers and colorants, or the like of any of them, or any other additive known in the art are further included in such compositions.

Please amend the specification at page 30 lines 11-13, as follows:

D16

In this version of the shuttle plasmid pSCΔE4, its expression is ~~furhter~~ further attenuated by Tet-KRAB, that binds to the E2 region in absence of tetracycline.

Please amend the specification at page 37 lines 5-8, as follows:

D17

In presence of doxycycline the E1 and E4 transcription activation can make cells permissive for viral replication, therefore evidencing the entailed ~~cytopatic~~ cytopathic effect.

Please amend the specification at page 38 lines 2-11, as follows:

The capacity of the cell clones including the episome pSCΔE4 of allowing replication of helper-dependent vectors can be studied ~~utilising~~ utilizing different vectors containing the reporter genes coding for the Green Fluorescent Protein (GFP) or for the ~~β-galattosidase~~ β-galactosidase or any other gene having an easily detectable activity. The cells can be infected with different moi of the helper-dependent virus, then harvested when the ~~cytopatic~~ cytopathic effect is evident, after tetracycline-induced expression of the adenoviral genome.

Please amend the specification at page 41 lines 16-19, as follows:

In presence of doxycycline the E1 and E4 transcription activation can make cells permissive for viral replication, therefore evidencing the entailed ~~cytopatic~~ cytopathic effect.